

## **REMARKS**

### **I. Status of the Claims.**

Claims 1-38 and 40-44 were pending. The present response cancels claims 15-17 and 36. Upon entry of the amendments, claims 1-14, 18-35, 37, 38 and 40-44 will be pending.

### **II. Description of the Amendments.**

Claims 3, 7-10, 13, 18-23, 25, 27-31 and 41-44 have been reworded to further enhance their clarity.

Claims 27 and 29 were amended to insert the definition of formula I from the specification into the claim.

Claim 38 was amended to insert Schemes 1 and 2 from the specification into the claim.

### **III. Response to the Office Action.**

#### **A. Allowable Subject Matter.**

Applicants note with appreciation that the Examiner has indicated that claim 14 is allowable.

Applicants also note that the Examiner has also indicated that claims 1-13 and 15-19 are clear of the art and that claims 1, 3, 5-7, 10-13 and 15-17 would be allowable if amended to overcome the rejections made under 35 U.S.C. § 101 and 112, second paragraph (which are addressed below). The Examiner also indicated that claims 2, 4, 8, 9, 18 and 19 were considered patentable, though objected to as being dependent on a rejected base claim.

Applicants are grateful for the foregoing indications of allowable subject matter.

#### **B. Objection to the Abstract of the Disclosure.**

The Abstract of the Disclosure was objected to as being allegedly "not in US format" and "excessively brief." Applicants note that an abstract of the disclosure need only provide "brief abstract of the technical disclosure" not exceeding 150 words in length. 37 C.F.R. § 1.72. Applicants have proposed an amendment to the Abstract. Should the Examiner continue to have any objections to the Abstract as amended, the Applicants would welcome the Examiner's

suggestions as to any further amendments to the text that would overcome any outstanding objections.

**C. Objection to the Disclosure.**

The Disclosure was objected to due to alleged errors.

It was alleged that Scheme 1 and Scheme 2 included spelling errors and that the quality of the structures was "rough." The objection is believed to be moot in view of the amendments made to the specification replacing these Schemes.

In claim 19, the term "nitro" was said to have been misspelled. The objection is believed to be moot in view of the amendment made to claim 19.

**D. Rejections of Claims 7, 13, 15-17, 20 and 21 under 35 U.S.C. § 101.**

Claims 7, 13, 15-17, 20 and 21 were rejected under 35 U.S.C. § 101. The rejection is moot as to claims 15-17, which have been cancelled. Applicants respectfully request reconsideration of the rejection as to claims 7, 13, 20 and 21.

The rejection states that the rejected claims recite a "use" without setting forth any steps in the process. Applicants respectfully disagree with what is apparently the Office's position that using the word "use" or "using" in claims is forbidden or inconsistent with a proper definition of steps involved in the process. For example, claim 7, 20 and 41 recites a step of "nitrating", while claim 13 recites "benzoylating." Nevertheless, solely to advance prosecution, applicants have amended the wording of claims 7, 13, 20 and 41 to render the objection moot.

**E. Rejections of Claims 1, 3, 5, 6, 8, 10-12, 19, 20, 22, 25-30, 32-34 and 43-44 under 35 U.S.C. § 112, second paragraph.**

Claims 1, 3, 5, 6, 8, 10-12, 19, 20, 22, 25-30, 32-34 and 43-44 were rejected under 35 U.S.C. § 112, second paragraph. Applicants respectfully request reconsideration of the rejection.

Applicants respectfully direct the Office to the guidance provided on the application of the definiteness requirement of 35 U.S.C. § 112, second paragraph provided in the MPEP. "The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. MPEP 2173. The focus during examination should be "whether the claim meets

the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available." MPEP 2173.02. "The requirement to 'distinctly' claim means that the claim must have a meaning discernible to one of ordinary skill in the art when construed according to correct principles. Only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite." *Id.* (quoting *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1366 (Fed. Cir. 2004)). In order to be found indefinite, the claims must be so insolubly ambiguous that no narrowing construction can properly be adopted. When a claim "is not insolubly ambiguous, it is not invalid for indefiniteness." *Bancorp v. Hartford Life*, 359 F.3d 1367, 1372 (Fed. Cir. 2004). Claims need not be plain on their face in order to avoid condemnation for indefiniteness; rather, what the examiner is asked is whether the claims are amenable to construction. *SmithKline v. Apotex*, 403 F.3d 1331, 1340 (Fed. Cir. 2005)(citing *Exxon Research & Engineering Corp. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001)). "If the language used by applicant satisfies the statutory requirements of 35 U.S.C. 112, second paragraph, but the examiner merely wants the applicant to improve the clarity or precision of the language used, the claim must not be rejected under 35 U.S.C. 112, second paragraph, rather, the examiner should suggest improved language to the applicant." MPEP 2173.02.

Applicants respectfully submit that many of reasons provided in the Office Action fail to establish that the claims are indefinite under the standards explained in the MPEP and summarized above. A common theme to many of the Office's remarks is that the Applicants have used generic terms for describing the processes claimed – which the Office characterizes as a failure to sufficiently *define* the claimed process. However, for none of the terms that the Office apparently finds objectionable (e.g. a process step of "converting," "reducing the amount," "recrystallizing," "nitrating" etc.) does the Office provide any explanation of why the use of such terms is considered to render the claims unclear or unsolvably ambiguous.

It appears from the Office Action's remarks that the Office is confusing the issues of clarity and enablement. Rather than explaining any way in which the meanings of the claims are unclear, the Office instead focuses on alleging that the Applicants have not limited their claims "sufficiently," e.g. by defining the particular reagents used to particular process steps. That is, the gravamen of the Office's observations appears to be that the claims do not define *how* the

claimed process must be performed, or that the claims are somehow too broad. However, the MPEP clearly explains that "[b]readth of a claim is not to be equated with indefiniteness" and that so long as "the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph.." MPEP 2173.04 (citing *In re Miller*, 441 F.2d 689 (CCPA 1971)). Furthermore, 35 U.S.C. § 112 second paragraph only requires that the claims define *what* is claimed, and not, for example, *how* the claimed process is carried out. The enablement requirement of 35 U.S.C. § 112 first paragraph requires that the *specification* describe *how* a claimed process may be carried out. However, there is no requirement that all such details must be specified in *the claims*.

Applicants therefore respectfully disagree, for the reasons explained in detail below, with many of the Office Action's contentions that the claims are unclear. If the Office continues to consider that any of the claims is unclear, and is inclined to maintain any of the indefiniteness rejections, applicants would welcome the Examiner's suggestions as to any amendments to the language of the claims which would improve their clarity and overcome the Examiner's objections, particularly if the Examiner can suggest language which would not unduly narrow the claims. The Examiner is invited to contact the undersigned to discuss any such suggestions.

Applicants provide a detailed response to each of the Office Action's remarks concerning the clarity of the claims below.

With respect to claim 1, the Office Action alleges "the term 'converting' standing alone is insufficient to adequately describe the process step or steps required to execute the claimed process wherein 2-nitropentabenzoyl adenosine is converted into the variety of 2-substituted adenosines encompassed by the subject matter disclosed at lines 3-8."

Applicants respectfully disagree that claim 1 is ambiguous by virtue of the use of the term "converting." The term "converting" does not, as the Office Action alleges, "stand alone" in defining the claimed process, but rather appears in conjunction definitions of the chemical structures of the starting material and product of the claimed "converting process." The claimed method describes a process which is converting a compound of a specific, defined structure (namely 2-nitropentabenzoyl adenosine) to a second compound (a 2-substituted adeosine) whose structure is also defined. Overall, the claim describes a specific synthetic route for preparing the

defined 2-substituted adenosines. The person skilled in the art can readily determine the scope of what is claimed, namely any process where 2-nitropentabenzoyl adenosine is chemically converted to form a 2-substituted adenosine meeting the definitions of formula I in claim 1: a process converting 2-nitropentabenzoyl adenosine to a compound of formula I is within the scope of the claim, whereas a process starting with a different starting material or ending with a different product is outside the scope of the claim. The metes and bounds of the claim are clear. Applicants respectfully submit, therefore, that the claim adequately and clearly defines the claimed process of converting 2-nitropentabenzoyl adenosine to form a 2-substituted of formula I, and that the Office Action has not pointed to anything in the language of the claim that can be considered to render the claim unclear or unresolvably ambiguous.

The Office Action alleges that claim 3 is unclear because the claim recited "converted .... by deprotecting." Applicants respectfully disagree that the claim was unclear for similar reasons to those set forth above. However, in order to improve the clarity of this claim even further by specifying that the conversion is performed by a process comprising reacting with C<sub>1-6</sub> alkoxide anion, or a phenoxide anion and deprotecting protected functional groups.

The Office Action alleges that claims 5, 6, 11, 12 and 22 are unclear because "the same or similar errors occur."

Applicants respectfully disagree, however, that any of claims 5, 6, 11 and 12 is unclear. Claim 5 recites a process further comprising "converting pentabenzoyl adenosine to 2-nitropentabenzoyl adenosine." Claim 6 recites a process further comprising "converting pentabenzoyl adenosine to 2-nitro-pentabenzoyl adenosine." Claims 11 and 12 each recites a process comprising "converting adenosine to pentabenzoyl adenosine." Each of these claims recites a process of converting one defined compound into another defined compound. Applicants respectfully submit such a recitation (i.e. "converting compound A to compound B") is not ambiguous or unclear in any respect. The claims define specific synthetic routes to the compounds described in each case. The person skilled in the art could readily determine whether any given process falls within or outside the scope of the claims by determining whether the process includes compound A being converted to compound B. The metes and bounds of the terms are perfectly clear, and the claim is therefore definite. The Office Action has not pointed

to anything in the language of any of these claims that properly can be considered unclear or unresolvably ambiguous.

For similar reasons, applicants disagree that claim 22 is unclear. The claim recites a process according to claim 20 (which defines a process of synthesizing a 2-substituted adenosine comprising, *inter alia*, producing a 2-substituted adenosine from 2-nitroadenosine pentaacetate) in which the 2-substituted adenosine is produced from 2-nitroadenosine pentaacetate by a process comprising deprotecting the 2-nitroadenosine pentaacetate and reaction with a C<sub>1-6</sub> alkoxide anion or a phenoxide anion. Applicants again respectfully submit that there is nothing unclear about this claim. The claim defines a specific synthetic route to compound 22. The person skilled in the art could readily appreciate that a process meeting the requirements of this claim would be one where 2-substituted adenosine is produced from 2-nitroadenosine pentaacetate by a process that includes both a deprotection of the 2-nitroadenosine pentaacetate (i.e. removal of the acetate groups) and a reaction with a C<sub>1-6</sub> alkoxide anion or a phenoxide anion. Thus, the metes and bounds of the claim are clear and the claim is definite. The Office Action again has not pointed to anything in the language of this claim that can be considered unclear or unresolvably ambiguous.

The Office Action alleges that claims 8 and 20 are unclear because the phrase "reducing the amount of TBAN or TMAN' is incomplete because the process step or steps being claimed have not adequately been described." Applicants again respectfully disagree that there is anything unclear in the term "reducing the amount of tetrabutylammonium nitrate or tetramethylammonium nitrate contaminating the resulting 2-nitroadenosine pentaacetate." The person skilled in the art would understand from reading the specification and claim that nitration of adenosine pentaacetate with one of the named tetraalkylammonium nitrates produces a product that contains the tetraalkylammonium nitrate as an impurity. The person skilled in the art would perfectly understand the meaning of the term "reducing the amount of tetrabutylammonium nitrate or tetramethylammonium nitrate contaminating the resulting 2-nitroadenosine pentaacetate" (namely making the amount lower) and whether a given process performs the recited step. The metes and bounds of the claim are clear and the claim is definite. The Office Action has not pointed to anything in the language of this term that causes the claims containing them to be unclear or unresolvably ambiguous.

The Office Action alleges that claims 10 and 19 are unclear because the claims recite a step of "recrystallising" a compound, but do not recite the presence of a solvent. Applicants respectfully disagree with the Office's assertion that omitting recitation of a solvent renders the claim in any way unclear or unresolvably ambiguous. Applicants respectfully point out that the method of recrystallization is a very commonly used technique for purification of compounds in organic chemistry in which a compound is brought into solution in a solvent, then caused to crystallize from the solution. It appears from the rejection that the Examiner well understands that a solvent would usually be used for such a recrystallization. Given this understanding, the Office fails to explain why reciting the presence of a solvent in these claim should be required in order to prevent the claim from being unclear or unresolvably ambiguous. Applicants respectfully submit that the Office does not explain why failure to recite the presence of a solvent would render a person skilled in the art unable to recognize whether, in a given process, a "recrystallisation" was performed. Applicants respectfully submit that the person skilled in the art could, in fact, readily recognize whether such recrystallisation is performed, and the metes and bounds of the claim are not rendered unclear by the fact that claims recites a step of "recrystallizing" without reciting the presence of a solvent.

The Office comments that in claim 22, it is unclear whether the deprotecting and reaction with alkoxide or phenoxide are both happening simultaneously and requests that applicants provide either a clarifying explanation or amendment. Applicants respectfully point out that the plain language of the claim recites that both deprotection and reaction with alkoxide or phenoxide occur in the claimed process. The reaction with an alkoxide or phenoxide introduces the R group of formula I. It is also possible that reaction with alkoxide or phenoxide could accomplish the required deprotection, such that both the "deprotecting" and "reaction with alkoxide or phenoxide" occur "simultaneously" in the same chemical operation. The claim, however, does not require or exclude the possibility that both the deprotecting and reaction with alkoxide or phenoxide could occur simultaneously.

The Office alleges that claim 25 is unclear because "the term 'acylated' appears twice but, because the products of the two process steps claimed are different, the process conditions must be different." The Office requests clarifications of the allegedly different meanings of the term "acylating" and alleges that claims 27, 29 and 43 raise the same concerns. Claim 25 recites a

process comprising two different acylating steps: acylation of adenosine to form a tri- and/or tetra-acetyl derivative, isolation of the intermediate, followed by further acylation of the intermediate to form adenosine pentaacetate. It is apparent from the language of the claim that the difference between the two acylating steps is that a different compound is acylated. The reaction conditions for effecting the two acylation steps could be the same or different. Applicants respectfully submit that the Office does not suggest any reason that a claim requiring acylation, isolation of an intermediate, and further acylation would be unclear or unresolvably ambiguous. Applicants respectfully submit that the person skilled would be able to determine whether or not such steps were performed in a given process, so that the metes and bounds of the claim are clear and the claim is not indefinite. Similar considerations apply with respect to claims 27 and 43. Claim 29 does not appear to recite two separate acylating steps.

The Office Action suggests that claim 26, 28, 29 and 44 are unclear because of their use of the term "washing." The Office alleges that the term is unclear because "the term 'washing' is generic with no particular details of the actual process step having been defined, and therefore the claimed process step is incompletely described." Applicants respectfully submit that the term "washing" is a commonly used term of ordinary meaning and that the person skilled in the art could readily determine whether a given process involves a washing step that removes adenosine tetraacetate as recited in these claims. The Office has not provided any reason to suggest why the use of the common term "washing" should be considered to render the claim unclear or unresolvably ambiguous.

The Office Action alleges that claims 27 and 29 are unclear because the specification refers to "formula I" but fails to define a chemical formula in the claim. For the same reason, the Office Action alleges that claims 28 and 30 are also unclear because these claims refer to the 2-substituted adenosine whose structure is undefined. Applicants have corrected these claims by inserting the definition of formula I from the specification into claims 27 and 29.

The Office Action alleges that claim 30 is incomplete because "the term 'nitrating' is incomplete because -- the reagent(s) -- required to effect this process step(s) has (have) not been disclosed in the claim, thereby rendering the claim incomplete." The Office Action alleges that Applicants respectfully point out that the term "nitrating" is not incomplete because it has a well-recognized meaning in the art, namely introducing a nitro group (usually via an electrophilic



substitution reaction). Applicants have specified that the process includes a nitrating step. Applicants respectfully disagree that the claim is "incomplete" because the particular reagents that can perform the nitrating process are not specified in the claim. Applicants claim a process in which a "nitrating step" is performed – not one where a nitration is performed with particular reagents. Applicants respectfully submit that the metes and bounds of the term "nitrating the adenosine pentaacetate to produce 2-nitroadenosine pentaacetate" would be perfectly clear to the person skilled in the art. The Office has not provided any reason to suggest why the metes and bounds of the claim would be unclear or unresolvably ambiguous to the person skilled in the art.

The Office Action alleges that claim 32 is unclear because "the process step whereby 2-nitroadenosine is converted into 2-chloroadenosine is claimed, but has not been described, thereby rendering the instant claimed process incompletely described in this claim." The Office alleges that claims 33 and 34 suffer from a "similar error." Applicants respectfully point out that these claims define process steps of "converting 2-nitroadenosine pentaacetate to 2-chloroadenosine pentaacetate," "converting 2-chloroadenosine pentaacetate to ... 2-substituted adenosine," "producing 2-chloroadenosine pentaacetate from 2-nitroadenosine pentaacetate." Applicants respectfully point out that the metes and bounds of these process steps are perfectly clear: the claim recites that one specific chemical is converted to another specific chemical. The claims do not require that any particular conditions be used. The Office has not provided any reason to suggest why the metes and bounds of the claim would be unclear or unresolvably ambiguous to the person skilled in the art. Accordingly, the claims are not indefinite.

The Office Action alleges that claim 38 was unclear because the claim referred to Scheme 1 and 2 without including the details of the Schemes in the claims. Claim 38 has been amended to include these Schemes.

The Office Action alleges that claims 41 was unclear due to the fact that they recited "TBAN" and "TMAN" rather than complete chemical names. This ground of rejection is moot because Applicants have amended the claim to recite the corresponding chemical names "tetrabutylammonium nitrate" and "tetramethylammonium nitrate."

The Office Action alleges that claim 41 was unclear because "the term 'reducing' implies a process step that has not been described with sufficient detail, thereby rendering this process step incompletely described in this claim" and that "the same error reoccurs" in claim 44.

Applicants respectfully point out that the Office Action completely fails to specify what it considers is unclear in this claim. Applicants respectfully point out the step referred to of “reducing the amount of tetrabutylammonium nitrate or tetramethylammonium nitrate” is a step whose metes and bounds are perfectly clear: the person skilled in the art would be able to recognize whether the claimed step has been performed by measuring the amount of TBAN or TMAN. The Office Action has not provided any explanation to indicate why the metes and bounds of these claims would be unclear or unresolvably ambiguous to the person skilled in the art. Accordingly, the claims therefore cannot be considered indefinite.

The Office Action alleges that claims 43 and 44 were unclear because “includes” was used as a transition phrase. This ground of rejection is moot because applicants have amended the claim to substitute the term “comprising.”

The Office Action also alleged that claims 43 and 44 were unclear because the preamble of the claims referred to three different processes but not explained how the body of the claim “fitted into” the claimed processes. Although applicants disagree the claims were unclear for this reason, applicants consider that the simplification of the preamble to these claims made in the amendment renders the ground of rejection moot.

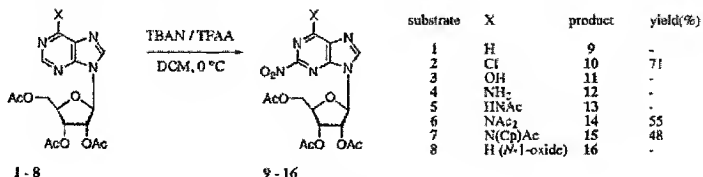
Based on the foregoing remarks, applicants respectfully submit that each of claims 1, 3, 5, 6, 8, 10-12, 19, 20, 22, 25-30, 32-34 and 43-44 as amended clearly define the boundaries of the claimed invention. These claims are not insolubly ambiguous or unclear, and therefore fully meet the requirements of 35 U.S.C. § 112 second paragraph. Applicants respectfully ask that the rejection of these claims made under 35 U.S.C. § 112 second paragraph be withdrawn.

**F. Rejections of Claims 20-38 and 40-44 under 35 U.S.C. § 102(b) As Being Allegedly Anticipated by Deghati.**

Claims 20-38 and 40-44 were rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Deghati *et al.*, *Tetrahedron Lett.* **2000**, *41*, 1291-95 (“Deghati”). The rejection is moot as to claim 36, which has been cancelled. Applicants respectfully traverse the rejection of claims 20-35, 37, 38 and 40-44.

The Office Action alleges that on page 1292, Scheme 1, and the associated explanatory text Deghati describes that “substrate 6 is nitrated to yield product 14 to yield product 14 when

contacted with tetrabutylammonium nitrate in the presence of trifluoroacetic anhydride, with subsequent deprotection yielding a mixture of 2-nitroadenosine and 2-methoxyadenosine." The Office Action alleges that the disclosure anticipates the rejected claims. For ease of reference, the relevant Schemes from Deghati are quoted below:



Scheme 1.

"A claim is anticipated only if *each and every element* as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP 2131 (citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)).

Applicants respectfully submit that the rejection is improper because the Office has not explained how Deghati describes each and every element of the rejected claims. Furthermore, Applicants respectfully submit that Deghati does not describe each and every element of the rejected claims and the rejected claims were not anticipated by Deghati.

Applicants provide detailed remarks as to each of the rejected claims below.

# 1. **Claim 40**

Claim 40 recites:

40. 2-methoxyadenosine *which is >96% pure*.

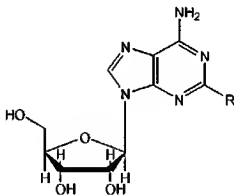
Applicants respectfully submit that the anticipation rejection of claim 40 is improper because the Office Action has failed to explain how Deghati describes each and every element of this rejected claim. Applicants respectfully submit that although the Office Action explains that Deghati describes 2-methoxyadenosine, the Office does not explain where Deghati describes 2-methoxyadenosine that is greater than 96% pure. In fact, according to the Office, Deghati only describes that 2-methoxyadenosine was prepared *as a mixture* with 2-nitroadenosine. Deghati does not provide any indication that the 2-methoxyadenosine was separated from the 2-

nitroadenosine, let alone that it was isolated with greater than 96% purity. In fact, the present application describes the limitations of the method of Deghati on page 3, explaining that when the method of Deghati is employed, the intermediate 2-nitroadenosine pentaacetate is contaminated with tetrabutylammonium nitrate or tetramethylammonium nitrate, and that this interferes with the subsequent methoxylation and deprotection of the 2-nitroadenosine pentaacetate. Thus, there is no evidence that 2-methoxyadenosine is inherently produced, of even that it could be produced, with greater than 96% purity employing the method described by Deghati. In fact, Deghati makes clear that the 2-methoxyadenosine produced is not pure, but rather is generated as a mixture with 2-nitroadenosine.

**2. Claim 20-26, 32 and 35.**

Claim 20 recites:

20. A method of synthesising a 2-substituted adenosine of formula I, which comprises: nitrating adenosine pentaacetate by reaction with tetrabutylammonium nitrate or tetramethylammonium nitrate to produce 2-nitroadenosine pentaacetate; *reducing the amount of tetrabutylammonium nitrate or tetramethylammonium nitrate contaminating the 2-nitroadenosine pentaacetate*; and then producing from the 2-nitroadenosine pentaacetate the 2-substituted adenosine according to formula I:



**I**

wherein R = C<sub>1-6</sub> alkoxy (straight or branched), a phenoxy group (unsubstituted, or mono-, or di-substituted by halo, amino, CF<sub>3</sub>-, cyano, nitro, C<sub>1-6</sub> alkyl, or C<sub>1-6</sub> alkoxy), a benzyloxy group (unsubstituted, or mono-, or di-substituted by halo, amino, CF<sub>3</sub>-, cyano, nitro, C<sub>1-6</sub> alkyl, or C<sub>1-6</sub> alkoxy), or a benzoyl group (unsubstituted, or mono-, or di-substituted by halo, amino, CF<sub>3</sub>-, cyano, nitro, C<sub>1-6</sub> alkyl, or C<sub>1-6</sub> alkoxy).

Applicants respectfully submit that the anticipation rejection of claim 20 is improper because the Office Action has failed to explain how Deghati describes each and every element of

this rejected claim. Specifically, the Office has not explained where a step of "reducing the amount of tetrabutylammonium nitrate or tetramethylammonium nitrate contaminating the 2-nitroadenosine pentaacetate" is described in the reference. It does not appear that Deghati describes any such step being performed.

The rejection of claims 21-26, 32 and 35 is improper, at least because these claims depend from, and therefore incorporate all the features of, claim 20. Additional reasons apply to render the rejections of claims 21, 23-26, 32 and 35 improper.

**a. Claim 21**

Claim 21 recites:

21. A method according to claim 20, *wherein the amount of tetrabutylammonium nitrate or tetramethylammonium nitrate contaminant is reduced by triturating the 2-nitroadenosine pentaacetate with isopropanol and washing the triturated 2-nitroadenosine pentaacetate with water.*

The rejection of claim 21 is also improper because the Office has failed to explain where Deghati describes that the amount of tetrabutylammonium nitrate or tetramethylammonium nitrate contaminant is reduced by triturating the 2-nitroadenosine pentaacetate with isopropanol and washing the triturated 2-nitroadenosine pentaacetate with water. It does not appear that Deghati describes any such triturating and washing steps being performed.

**b. Claim 23**

Claim 23 recites:

23. A method according to claim 20, wherein the 2-substituted adenosine is 2-methoxyadenosine, and the 2-methoxyadenosine is produced from the 2-nitroadenosine pentaacetate by *reacting the 2-nitroadenosine pentaacetate with methoxide anion from methanol/NaOMe, methanol/n-BuLi, methanol/NaOH, methanol/NaH, or methanol/KO<sup>t</sup>Bu.*

The rejection of claim 23 is also improper because the Office has failed to explain where Deghati describes that the 2-methoxyadenosine is produced from the 2-nitroadenosine pentaacetate by reaction with methoxide anion from methanol/NaOMe, methanol/n-BuLi, methanol/NaOH, methanol/NaH, or methanol/KO<sup>t</sup>Bu. The 2-methoxyadenosine in Deghati is produced by reaction with potassium cyanide/methanol. It does not appear that Deghati in fact describes any of the reagents specified in claim 23 being used.

**c. Claim 24**

Claim 24 recites:

24. A method according to claim 20, which further comprises *synthesizing the adenosine pentaacetate by acylating adenosine*.

The rejection of claim 24 is also improper because the Office has failed to explain where Deghati describes synthesizing adenosine pentaacetate by acylating adenosine. It does not appear that Deghati describes how compound 6 therein was prepared.

**d. Claim 25**

Claim 25 recites:

25. A method according to claim 24, wherein the *adenosine is acylated to form an O-tri-acetyl and/or tetra-acetyl derivative of adenosine, the derivative(s) is isolated, and the isolated derivative(s) is further acylated to produce adenosine pentaacetate*.

The rejection of claim 25 is also improper because the Office has failed to explain where Deghati describes synthesizing adenosine pentaacetate by acylating adenosine by a process comprising acylating adenosine, isolating a tri- or tetra-acylated intermediate, and further acylating the intermediate. As noted above, it does not appear that Deghati describes how compound 6 therein was prepared.

**e. Claim 26**

Claim 26 recites:

26. A method according to claim 24, which further comprises *washing the adenosine pentaacetate to remove contaminating adenosine tetraacetate before nitrating the washed adenosine pentaacetate to form the 2-nitroadenosine pentaacetate*.

The rejection of claim 26 is also improper because the Office has failed to explain where Deghati describes washing the adenosine pentaacetate to remove contaminating adenosine tetraacetate before nitrating the washed adenosine pentaacetate to form the 2-nitroadenosine pentaacetate.. As noted above, it does not appear that Deghati provides any details as to how compound 6 therein was prepared.

**f. Claim 32**

Claim 32 recites:

32. A method according to claim 20, which further comprises *converting 2-nitroadenosine pentaacetate to 2-chloroadenosine pentaacetate* before producing the 2-substituted adenosine from the 2-chloroadenosine pentaacetate.

The rejection of claim 32 is also improper because the Office has failed to explain where Deghati describes 2-nitroadenosine pentaacetate to 2-chloroadenosine pentaacetate. It does not appear that Deghati describes such a conversion.

**g. Claim 35**

Claim 35 recites:

35. A method according to claim 32, wherein the 2-substituted adenosine is 2-methoxyadenosine, and the *2-chloroadenosine pentaacetate is converted to 2-methoxyadenosine* by reaction with methoxide anion from methanol/NaOMe, methanol/n-BuLi, methanol/NaOH, or methanol/NaH with the 2-nitroadenosine pentaacetate.

The rejection of claim 35 is also improper because the Office has failed to explain where Deghati describes 2-chloroadenosine pentaacetate being converted to 2-methoxyadenosine as required by the claim. It does not appear that Deghati describes such a conversion.

**3. Claims 27, 28, 30 and 31**

Claim 27 recites:

27. A method of synthesising a 2-substituted adenosine of formula 1 ... wherein the method *comprises acylating adenosine to form an O-tri-acetyl and/or tetra-acetyl derivative of adenosine, isolating the derivative(s), further acylating the isolated derivative(s)* to produce adenosine pentaacetate, and producing the 2-substituted adenosine from the adenosine pentaacetate.

Applicants respectfully submit that the anticipation rejection of claim 27 is improper because the Office Action has failed to explain how Deghati describes each and every element of this rejected claim. Specifically, the Office has not explained where Deghati describes synthesizing adenosine pentaacetate by acylating adenosine by a process comprising acylating adenosine, isolating a tri- or tetra-acylated intermediate, and further acylating the intermediate. As noted above, it does not appear that Deghati describes how compound 6 therein was prepared.

The rejection of claim 28, 30 and 31 is improper, at least because these claims depend from, and therefore incorporate all the features of, claim 27. Additional reasons apply to render the rejections claims 28 and 31 improper.

**a. Claim 28**

Claim 28 recites:

28. A method according to claim 27 which further comprises *washing the adenosine pentaacetate to reduce the amount of contaminating adenosine tetraacetate* before producing the 2-substituted adenosine of formula I from the washed adenosine pentaacetate.

The rejection of claim 28 is also improper because the Office has failed to explain where Deghati describes adenosine pentaacetate being washed to reduce the amount of contaminating adenosine tetraacetate as required by the claim. It does not appear that Deghati in fact describes adenosine pentaacetate being washed in this way.

**b. Claim 31**

Claim 31 recites:

31. A method according to claim 30, wherein the 2-substituted adenosine is 2-methoxyadenosine, and *the 2-methoxyadenosine is produced by reacting methoxide anion from methanol/NaOMe, methanol/n-BuLi, methanol/NaOH, methanol/NaH, or methanol/KO<sup>t</sup>Bu with the 2-nitroadenosine pentaacetate.*

The rejection of claim 31 is also improper because the Office has failed to explain where Deghati describes 2-methoxyadenosine being produced by reacting methoxide anion from methanol/NaOMe, methanol/n-BuLi, methanol/NaOH, methanol/NaH, or methanol/KO<sup>t</sup>Bu with the 2-nitroadenosine pentaacetate. It does not appear that Deghati in fact describes 2-methoxyadenosine being produced in this way.

**4. Claim 29**

Claim 29 recites:

29. A method of synthesising a 2-substituted adenosine of formula I ... wherein the method comprises *acylating adenosine, or an acylated derivative of adenosine, to form adenosine pentaacetate, washing the adenosine pentaacetate to reduce the amount of contaminating adenosine tetraacetate*, and producing the 2-substituted adenosine of formula I from the washed adenosine pentaacetate.



Applicants respectfully submit that the anticipation rejection of claim 29 is improper because the Office Action has failed to explain how Deghati describes each and every element of this rejected claim. Specifically, the Office has not explained where Deghati describes that adenosine pentaacetate is prepared by acylating adenosine or an acylated derivative of adenosine. Neither has the Office explained where Deghati discusses washing the adenosine pentaacetate to reduce the amount of contaminating adenosine tetraacetate as recited in the claim. As noted above, it does not appear that Deghati describes how compound 6 therein was prepared or that a washing step was performed.

**5. Claims 33 and 34**

Claims 33 and 34 recite:

33. A method of synthesising a 2-substituted adenosine, which comprises *converting 2-chloroadenosine pentaacetate to the 2-substituted adenosine.*

34. A method according to claim 33, which further comprises *producing the 2-chloroadenosine pentaacetate from 2-nitroadenosine pentaacetate.*

Applicants respectfully submit that the anticipation rejection of claims 33 and 34 is improper because the Office Action has failed to explain how Deghati describes each and every element of these rejected claims. Specifically, the Office has not explained where Deghati describes converting 2-chloroadenosine pentaacetate to a 2-substituted adenosine. Neither has the Office explained where Deghati discusses washing the adenosine pentaacetate to reduce the amount of contaminating adenosine tetraacetate as recited in the claim. As noted above, it does not appear that Deghati describes how compound 6 therein was prepared or that a washing step was performed.

**6. Claim 37**

Claim 37 recites:

37 A method of synthesising 2-methoxyadenosine, which comprises *reacting methoxide anion from methanol/NaOMe, methanol/n-BuLi, methanol/NaOH, methanol/NaH, or methanol/KO<sup>t</sup>Bu with 2-nitroadenosine pentaacetate.*

Applicants respectfully submit that the anticipation rejection of claim 37 is improper because the Office Action has failed to explain how Deghati describes each and every element of this rejected claim. Specifically, the Office has not explained where Deghati describes that

methoxide anion from methanol/NaOMe, methanol/n-BuLi, methanol/NaOH, methanol/NaH, or methanol/KO<sup>t</sup>Bu is reacted with 2-nitroadenosine pentaacetate. It does not appear that Deghati describes such a reaction.

**7. Claim 38**

Claim 38 recites:

38 A method of synthesising 2-methoxyadenosine, which comprises *the steps shown* in scheme 1 or 2...

Applicants respectfully submit that the anticipation rejection of claim 38 is improper because the Office Action has failed to explain how Deghati describes each and every element of this rejected claim. Specifically, the Office has not explained where Deghati describes a method of synthesizing 2-methoxyadenosine comprising each of the steps in Scheme 1 or 2. It does not appear that Deghati describes such a method.

**8. Claims 41 and 42**

Claims 41 and 42 recite:

41. A method of synthesising 2-nitroadenosine pentaacetate, which comprises nitrating adenosine pentaacetate by reaction with tetrabutylammonium nitrate or tetramethylammonium nitrate to produce 2-nitroadenosine pentaacetate, and *reducing the amount of tetrabutylammonium nitrate or tetramethylammonium nitrate contaminating the 2-nitroadenosine pentaacetate.*

42. A method according to claim 41, wherein the amount of tetrabutylammonium nitrate or tetramethylammonium nitrate contaminant is reduced by *trituration of the 2-nitroadenosine pentaacetate with isopropanol and washing the trituration 2-nitroadenosine pentaacetate with water.*

Applicants respectfully submit that the anticipation rejection of claims 41 and 42 is improper because the Office Action has failed to explain how Deghati describes each and every element of these rejected claims. Specifically, the Office has not explained where Deghati describes a method of synthesizing 2-nitroadenosine pentaacetate in which a step of reducing the amount of tetrabutylammonium nitrate or tetramethylammonium nitrate contaminating the 2-nitroadenosine pentaacetate is performed. Furthermore, the rejection of claim 42 is improper because the Office has not explained where Deghati describes that such a step is performed by trituration of the 2-nitroadenosine pentaacetate with isopropanol and washing the trituration 2-

nitroadenosine pentaacetate with water. It does not appear that Deghati describes such a method including such a step.

**9. Claim 43**

Claim 43 recites:

43 A method of synthesising adenosine pentaacetate comprising the following steps: *acylating adenosine to form an O-tri-acetyl and/or tetra-acetyl derivative of adenosine, isolating the derivative(s), and further acylating the isolated derivative(s)* to produce adenosine pentaacetate.

Applicants respectfully submit that the anticipation rejection of claim 44 is improper because the Office Action has failed to explain how Deghati describes each and every element of this rejected claim. Specifically, the Office has not explained where Deghati describes a step of preparing adenosine pentaacetate in which the steps of acylating adenosine to form a tri- and/or tetra-acetyl derivative of adenosine is formed, isolated and further acylated to produce adenosine pentaacetate. As noted above, Deghati does not discuss how compound 6 therein was formed.

**10. Claim 44**

Claim 44 recites:

44 A method of synthesising adenosine pentaacetate comprising the following steps: *acylating adenosine or an acylated derivative of adenosine to form adenosine pentaacetate; and washing the adenosine pentaacetate to reduce the amount of contaminating adenosine tetraacetate.*

Applicants respectfully submit that the anticipation rejection of claim 44 is improper because the Office Action has failed to explain how Deghati describes each and every element of this rejected claim. Specifically, the Office has not explained where Deghati describes a step of preparing adenosine pentaacetate in which the steps of acylating adenosine or an acylated derivative of adenosine to form adenosine pentaacetate; and washing the adenosine pentaacetate to reduce the amount of contaminating adenosine tetraacetate are performed. As noted above, Deghati does not discuss how compound 6 therein was formed.

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#### IV. Conclusion.

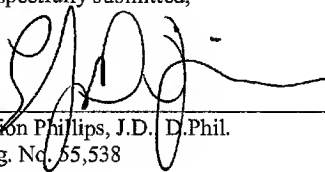
Based on the foregoing, the applicants believe that the rejections have been overcome. It is respectfully submitted that the application should be found in condition for allowance, and an early notice toward that end is earnestly solicited.

Please charge any required fees or apply any credits to Deposit Account No. 06-1050 referencing Attorney Docket No. 13425-0192US1.

Date: \_\_\_\_\_

10/29/2009

Respectfully submitted,



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